

In the specification

Please insert the following paragraph on page 1 below the title and above the heading
“Background of the Invention”:

This application is a continuation of Serial No. 09/403,428 filed January 6, 2000, entitled
“Multifunctional Polymeric Tissue Coatings”, by Jeffrey A. Hubbell, Donald L. Elbert, and
Curtis B. Herbert, which is a filing under 35 USC §371 of PCT Application No.
PCT/US98/07590 filed April 17, 1998, which claims priority to U.S.S.N. 60/044,733 filed on
April 18, 1997.

Please replace the paragraph on page 3, lines 2-25, with the following paragraph.

Compositions for encapsulating cells and for coating biological and non-biological
surfaces, which minimize or prevent cell-cell contact and tissue adhesion, and methods of
preparation and use thereof, are disclosed. Embodiments include polyethylene glycol/polylysine
(PEG/PLL) block or comb-type copolymers with high molecular weight PLL (greater than 1000,
more preferably greater than 100,000); PEG/PLL copolymers in which the PLL is a dendrimer
which is attached to one end of the PEG; and multilayer compositions including alternating
layers of polycationic and polyanionic materials. In the PEG/PLL dendrimers, the molecular
weight of the PLL is between 1,000 and 1,000,000, preferably greater than 100,000, more
preferably, between 300,000 and 800,000, and the molecular weight of the PEG is between 500
and 2,000,000, preferably greater than 50,000, more preferably between 5,000 and 100,000. For
PEG of MW 5000, the optimal ratio is between 1 PEG chain for every 3 to 10, preferably 5 to 7,

lysine subunits. The optimal ratio for PEG of a molecular weight other than 5000 can be determined using routine experimentation, for example, using the procedures outlined in Example 1. In general, PEG/PLL grafts of various ratios are synthesized, for example, by varying the relative stoichiometric amounts of each component used in a suitable coupling reaction, and their relative efficacy in preventing a model binding interaction can then be determined. One method for doing this involves determine the extent of cell spreading on an anionic polystyrene surface, either uncoated or coated with the polymers.

Please replace the paragraph on page 7, lines 2-8, with the following paragraph.

The PEG/PLL co-polymers can be brush copolymers (as in a bottle brush, with a backbone of one composition and bristles of another) with a backbone of polylysine (PLL) and bristles of polyethylene glycol (PEG). The molecular weight of the PLL is between 1,000 and 1,000,000, preferably greater than 100,000, more preferably, between 300,000 and 800,000. The molecular weight of the PEG is between 500 and 2,000,000, preferably greater than 50,000, more preferably between 5,000 and 100,000.

Please replace the paragraph on page 14, lines 5-22, with the following paragraph:

An example of a suitable ligand is the pentapeptide Tyr-Ile-Gly-Ser-Arg (YIGSR) (SEQ ID NO:1), which supports endothelial, smooth muscle cell, and fibroblast adhesion, but not platelet adhesion; or the tetrapeptide Arg-Glu-Asp-Val (REDV) (SEQ ID NO:2), which has been shown to support endothelial cell adhesion but not that of smooth muscle cells, fibroblasts, or platelets, as described in Hubbell, et al., *BioTechnology* 9:568-572 (1991). YIGSR

(SEQ ID NO:1), from laminin, binds to receptors on endothelial cells, but not on blood platelets.

This, the conjugation of the oligopeptide YIGSR (SEQ ID NO:1) to the termini of the (A)_x and adsorbing the polymeric material to a damaged vessel wall would be expected to block thrombosis on the vessel wall but not to block re-endothelialization from the surrounding undamaged vessel wall. This embodiment makes it possible to cover an injured vessel wall to prevent thrombosis but, via an adhesion ligand on the termini of one or more of the polymeric components, to permit the regrowth of endothelial cells upon the polymer. This approach also permits the re-endothelialization of the vessel wall while it is still not adhesive to platelets, thus enabling healing while avoiding platelet activation and thrombus formation.

Please replace the paragraph on page 37, lines 5-16, with the following paragraph:

Peptides were attached via their N-terminal amines to the carboxyl side chains of polyacrylic acid (MW 250,000) (PAA) with N,N,N',N'-tetramethyluronium tetrafluoroborate (TSTU). Activated PAA was prepared by combining 200 μ l of 20 mg/ml PAA in anhydrous DMF with 40 μ l of 50 mg/ml TSTU and 20 μ l of di-isopropyl ethylamine (DIPEA) to achieve a mixture with 61 μ mol PAA COOH moieties, 6.7 μ mol TSTU and 121 μ mol DIPEA. A solution of peptide in buffer was added dropwise to the activated PAA. The peptide-PAA crude mixture was purified of unbound peptides by dialysis. The samples were lyophilized. This process was performed as described with the Arg-Gly-Asp (RGD-), Arg-Asp-Gly (RDG-), Tyr-Ile-Gly-Ser-Arg (YIGSR-) (SEQ ID NO:1), ~~an~~ and His-Ala-Val (HAV-) containing peptides.

Continuation of U.S.S.N. 09/403,428
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Please amend the application by inserting the attached one (1) page of Sequence Listing
after the drawings and declaration.